The Examiner has rejected Claims 6-9, 19, 20, 22, and 23 under 35 USC § 112, second paragraph. Applicants have amended these claims in order to further clarify the present invention and advance prosecution of the present application by deletion of the term "about". Accordingly, withdrawal of the present rejection of these claims under Section 112 is respectfully requested.

The Examiner has rejected Claims 1, 2, 6, 7, 18, 19 and 20 under 35 USC Section 103(a) as allegedly rendered unpatentable by Hillman et al in view of Prevost et al. Claims 10, 12, 14 and 16 have been rejected under 35 USC Section 103(a) as allegedly rendered unpatentable by Hillman et al in view of Prevost et al and Wilding et al. Claims 3, 5, 8, 9, 21, 22 and 23 have been rejected under 35 USC Section 103(a) as allegedly rendered unpatentable by Hillman et al in view of Prevost et al and further in view of Mansky et al and Wilding et al. Claim 4 has been rejected under 35 USC Section 103(a) as allegedly rendered unpatentable by Hillman et al in view of Prevost et al and further in view of Mansky et al and Yassinzadeh et al. None of these references, neither singly nor in combination, teach or suggest the claimed invention.

Hillman et al disclose using filtration techniques within a chamber. Hillman et al discuss the removal of red blood cells from a liquid phase. In col. 7, lines 54 to 58, Hillman et al note that "by employing various filtration or trapping devices (e.g., mechanical or magnetic), one can inhibit the transfer of particles from a capillary channel to a chamber or vice versa. In this way, red cells can be removed from blood." In col. 9, lines 17 to 19, Hillman et al state that, "where the sample is colored, such as blood, it may be necessary to filter out or trap red blood cells." Also in col. 9, lines 36 to 38, Hillman et al sets forth that "by having a filter at the exit of the second unit, all of the particles will be trapped at the filter."

The claimed invention is entirely different from the disclosure of Hillman et al. Hillman et al is aiming at the ***total*** removal of particles such as red blood cells from a liquid sample, by using a filter of very small pore size. In contrast to Hillman et al, the present invention is directed to the production of monolayers of particles in low concentration ***behind*** a separation wall within a chamber. In other words, the method of the present invention would not be achieved if "all of the particles would be trapped" at the separation wall. Instead, in the present invention, an inventive separation wall

has been designed and used that comprises two different types of separation channels, whereby one type is sized so that particles such as red blood cells can freely pass through, whereas the other type is sized so that only liquid may pass through. In the present invention, by selecting appropriate dimensions for both types of separation channels, a desired degree of reduction in the particle concentration in the chamber behind the separation wall can be achieved reproducibly, whereby the degree of reduction is selected so that, in combination with an appropriate chamber height behind the separation wall, a monolayer of particles such as red blood cells is obtained. Moreover, the effect of a controlled reduction in particle concentration could not be achieved by using only the one type of separation channel that lets particles pass through. In this case, the liquid portion would also pass the separation channel, and the concentration of the particles in the liquid would not change. Applicants respectfully submit that these aspects of the claimed invention are not disclosed in Hillman et al. Consequently, it would not have been obvious at the time the invention was made, in view of Hillman et al., to use the two specific types of separation channels in a separation wall.

The secondary reference Prevost et al is directed at resolving the problem of preventing the clogging of membranes due to the accumulation of particles that are retained at the pores of said membranes. Prevost et al teach the use of means for (i) canalizing a current of a mixture of a continuous phase (e.g. a liquid) and a disperse phase (e.g. particles), and (ii) suited for communicating thereto a helical motion of the mixture along a central shaft, the helical motion leading to a differentiated radial displacement of the continuous phase and of the disperse phase under the action of the centrifugal force, during which the continuous phase flows through a filtration means such as a membrane, whose pore size is markedly smaller than the size of the particles to be retained (col. 2, lines 29 to 39; col. 9, line 55 to col. 10, line 6; and col. 1, lines 46 to 48). In other words, Prevost et al use filtration walls such as common membranes of small pore size that are holding back ***all*** particles. The inventive step is directed at the prevention of membrane clogging. This goal is achieved by generating a liquid flow pattern that directs the particles away from the membrane by applying centrifugation. Applicants respectfully submit that the teachings of Prevost et al do not

teach or suggest the use of two types of separation channels in a separation wall in order to obtain a monolayer of particles behind said separation wall.

The Examiner has alleged that the primary reference Hillman et al disclose notches and vanes in the embodiment of Fig. 1b for ***causing turbulence***. As is outlined in the present application (page 8, col. 13 to 21), notches are displaced laterally across the flow path of the liquid sample to achieve an opposite goal, i.e. to "even out" the flow front of the sample. The notches in the present application obtain a more laminar flow of the liquid sample towards the separation wall. This stands in clear contrast to Hillman et al's goal of causing turbulence within the liquid sample. Consequently, Applicants respectfully submit that the use of notches and vanes in Hillman et al do not render obvious the use of notches in the claimed invention.

The Examiner has alleged that the secondary reference Wilding et al teaches using notches and piercing protrusions in a cell-lysing chamber. These protrusions form a filter 28 "to enable the removal of the lysed cell membrane and other cell debris components from the sample" (col. 7, lines 29 to 34). As in Hillman et al, such a filter is intended to remove ***all*** particulate debris from the liquid sample. Therefore, Applicants respectfully submit that the secondary reference Wilding et al adds no additional teachings with Hillman et al and Prevost et al (or with any other combination of the cited prior art) at the time the invention was made to lead one of ordinary skill in the art to use two types of separation channels to obtain a decreased (but not zero) particle concentration in a liquid sample ***behind*** a separation wall.

As the Examiner points out, the secondary reference Mansky et al discloses a method of material characterization using a moat surrounding a sample chamber ***to provide thermal isolation*** (col. 16, lines 25 to 30). In the method of the present invention, a moat around the sample chamber is provided for a totally different purpose. The purpose in the present invention is to provide an open space outside of the sample chamber so that during the filling of the chamber with a liquid sample the air that is inside can be pressed through the venting channels to the outside, allowing for a complete filling of the sample chamber (see Page 7 of the present application, Lines 25 to 28). It is important for the functioning of the method according to the present invention that the moat stays free, in particular also free of liquid sample,

during its use. For the case that some liquid enters the moat area, it is important that this liquid portion does not fill the whole moat and hereby block said venting channels. This is accomplished by providing specifically designed capillary stops (14), (15), and (16) within the moat (see Page 9 of the present application, Lines 1 to 7). Thus the secondary reference Mansky et al provides no additional teachings that disclose or suggest the claimed invention.

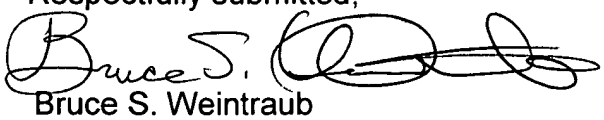
In Yassinzadeh et al, "configurations which create capillary stops" (col. 1, lines 23 to 24) are mentioned as a problem, but no specific structures are disclosed that would prevent the flow of liquid intentionally. Applicants respectfully submit that neither Yassinzadeh et al nor Mansky et al, nor both together in combination with Hillman et al and Prevost et al could have made it obvious at the time the present invention was made to one of ordinary skill in the art to keep venting channels in the walls of a sample chamber open by placing a moat with specific capillary stops around the chamber.

Accordingly, the primary reference Hillman et al does not teach or suggest the claimed invention, and Hillman et al in combination with the secondary references (respectively (1) Prevost et al; (2) Prevost et al and Wilding et al; (3) Prevost et al, Mansky et al and Wilding et al; and (4) Prevost et al, Mansky et al and Yassinzadeh et al) do not teach or suggest the claimed invention.

Thus, the claims of the present application are believed to be in condition for allowance. Early notice thereof is respectfully requested by Applicants.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 6-9, 19, 20, 22 and 23 have been amended as follows.

6. (Amended) The method according to Claim 1 wherein said first separation channel is [about] 3 to 10 μm deep to 5 to 50 μm wide.

7. (Amended) The method according to Claim 1 wherein said second separation channel is [about] 0.5 to 1.5 μm deep by 50 to 1000 μm wide.

8. (Amended) The method according to Claim 3 wherein said first separation channel is [about] 3 to 10 μm deep by 5 to 50 μm wide.

9. (Amended) The method according to Claim 3 wherein said second separation channel is [about] 0.5 to 1.5 μm deep by 50 to 1000 μm wide.

19. (Amended) The method of Claim 1 wherein said second compartment has a thickness of from [about] 1 to 7 μm.

20. (Amended) The method of Claim 1 wherein said first compartment has a thickness of from [about] 10 to 50 μm.

22. (Amended) The method of Claim 3 wherein said second compartment has a thickness of from [about] 1 to 7 μm.

23. (Amended) The method of Claim 3 wherein said first compartment has a thickness of from [about] 10 to 50 μm.